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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,115	09/10/2003	Jonathan Axon	219002029400	6854

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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	
ART UNIT	**PAPER NUMBER**
1624	

DATE MAILED: 08/25/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Advisory Action Before the Filing of an Appeal Brief	Application No. 10/660,115	Applicant(s) AXON ET AL.	
	Examiner Venkataraman Balasubramanian	Art Unit 1624	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 15 August 2006 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☐ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires 3 months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: *21 and 23*.
   Claim(s) rejected: *1-20 and 22*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☐ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: _____.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08 or PTO-1449) Paper No(s). _____
13. ☒ Other: See attached Advisory Action.

Venkataraman Balasubramanian
Primary Examiner
Art Unit: 1624

8/28/06

ADVISORY ACTION

The applicants' response, which included amendment to claims, filed 8/15/2006 under 37 CFR 1.116 in reply to the final rejection has been considered but is not deemed to place the application in condition for allowance for the following reasons.

In view of applicants' response, the following rejections made in the previous office action are maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 20 is rejected under U.S.C. 112, first paragraph, because the specification while being enabling for treating fibrosis of liver, does not reasonably provide enablement for treating any or all diseases or conditions mediated by TGFβ generically embraced in the claim language for reasons of record.

Applicants' amendment to limit the claim to fibroproliferative disorder or cancer did not overcome this rejection for reasons of record.

To repeat, as noted in the previous office action, instant claims, as recited, are reach through claims. A reach through claim is a claim drawn to a mechanistic, receptor binding or enzymatic functionality in general format and thereby reach through a scope of invention for which they lack adequate written description and enabling disclosure in the specification.

In the instant case, based on the inhibition of TGFβ by the instant compounds,

instant claims reaches through inhibiting and treating any or all fibroproliferative disorder or cancer in general and thereby they lack adequate written description and enabling disclosure in the specification.

More specifically, in the instant case, based on the mode of action of instant compounds as inhibitor of TGFβ, based on limited assay, it is claimed that treating any or all fibroproliferative disorder including any or all cancers in general, which there is no enabling disclosure.

Applicants' argument is also clearly indicative of emphasis on the mode of action and then reaching through to treat any or all diseases based on the mode of action.

The references submitted by the applicants as exhibits A-D were considered. Careful analysis would show that these are again would provide support for treating any or all fibroproliferative disorders or cancers.

Hence, based on these considerations, the rejection is deemed as proper and is maintained.

Claim Rejections - 35 USC § 102

Claims 1-18, 20, 21 and 22 are rejected under 35 U.S.C. 102(b) as being anticipated by Cai et. al. WO 02/47690 .

In view of applicants' pointing out each the species pointed out that instant claims require a phenyl at 2-position, while species of Cai et al. have pyridyl group, this rejection has been deemed as obviated.

Claim Rejections - 35 USC § 103

Claims 1-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cai et al., WO 02/47690. This rejection has been deemed as obviated for reasons stated in the above 102 rejection.

Claims 1-19 and 22 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kleemann et al., US 5,849,758 for reasons of record.

This rejection is same as made in the previous office action. In the previous response, although applicants' amendment to exclude O from X definition obviated the 102 rejection, in view of equivalency teaching of X as O with X as S in Kleemann, this rejection was maintained.

In this response, applicant argued that the fact that O and S are Markush choices does not make them equivalent. This an incorrect analysis and is not persuasive.

First of all, it is noted that applicants X is NR^1 or S and specification has only $N(R^1)$-Ar compounds not the S analog. Based on applicants' argument, it appears that applicants have no enablement of the use of the compounds as well as process of making. Applicants appear to use two different standards. Page45 exampl14 of instant specification states instant compounds are active in the range of .05-50 micromolar

concentrations. Does this mean that above certain limit in the said range instant compounds teaches away from $N(R^1)Ar$ compounds ?

Secondly, the above said statement in Kleemann et al. is as good as instant statement of range of activity and does not teach away from the instant Markush choices. It merely points out some of O analogs had good activity. As much as instant specification shows variation among the compounds made, the reference compounds can also have such variations and it cannot by no means construed that all S analogs lack desired activity.

Thirdly, in this regard applicants' attention is drawn to In re Bruckel which states " References must be considered under 35 U.S.C 103, not only for what it expressly teaches but also for what it fairly suggests; all disclosures of prior art, including unpreferred embodiments must be considered in determining obviousness". In re Bruckel, 201 USPQ 67.

The equivalency teaching of X =O with X= S, should therefor given due consideration as much as instant Markush choices mentioned above.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for

the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

Venkataraman Balasubramanian

8/25/2006